## REMARKS

Entry of this amendment and reconsideration and allowance of the subject application as amended, are respectfully requested. The amendments proposed herein raise no new issues and are believed to place the application in condition for allowance.

The claims have been amended to specify that the method relates to <u>total</u> nucleic acid in the sample (regardless of source, size, sequence, etc.) Basis for the claim amendments can be found throughout the specification, e.g. page 8.

Claims 1-3, 6-12, 14-25, 28-32 and 34-37 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Hartley (5,043,272) in view of Eberle et al (5,413,906). Reconsideration is requested.

The present invention provides a sensitive method for measuring total nucleic acid in a sample. The cited references do not disclose or predict the surprising <u>in</u>sensitivity of the present invention to the source, size, sequence and heterogeneity of the nucleic acid in the sample.

Specific replies to the Examiner's comments are presented below:

a. "However, the disclosure of Hartley indicates that the amplification can be performed without prior knowledge of specific sequence, the method can be used for detection, and the method may also be desirable in the quantitation of the amplified product." Hartley does disclose amplification without prior knowledge of specific sequence, but does not disclose detection or quantitation without prior knowledge of specific sequence or detection and quantitation of total nucleic acid in a sample. As noted previously, all the examples of nucleic acid quantitation in Hartley use a specific nucleic acid probe so as to specifically detect only a single sequence. There is no indication in Hartley that amplification will be independent of source/size/sequence, etc.

- b. "Eberle et al do disclose that the method can be used for detection." As described in the last response, Eberle is a method for measuring polymerase activity through the use of a well defined template strand of nucleic acid. There is no indication that the signal obtained from the Eberle assay would be independent of nucleic acid size/sequence/complexity, etc. as is the case in the present invention.
  - c. "it is unclear whether the method is for detection or quantitation or both." It is both.
- d. "The nucleic acid used in the instant invention is not specified by that the nucleic acid is a specific nucleic acid or an unknown sequence." The claims have been amended to state that the method relates measuring total nucleic acid in the sample. This clearly distinguishes the subject method from the cited art.

Claims 4, 5, 13, 26, 27 and 33 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Hartley (5,043,272) in view of Wu et al and Respess (5,599,662). Reconsideration is requested.

The Examiner's rejection requires that a ligated nucleic acid product be considered to have a "binding species" since it can bind to a complementary probe. One of skill in the art, on reading the present specification would understand that a "binding species" is not the ligated nucleic acid itself (i.e., not the sequence complementary to the target sequence in the sample) but a moiety that is introduced into the product by attachment to one of the primers.

Claim 38 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Hartley in view of Eberle et al. Reconsideration is requested.

Claim 38 has been amended to clearly distinguish the method from Hartley and Eberle for the reasons noted above.

Claims 39-40 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Hartley in view of Wu. Reconsideration is requested.

The amendments noted above obviate this rejection.

In view of the above, Applicants respectfully submit that if the claims are amended as above, they would fully and patentably define the present invention over the applied art of record. As such, early receipt of the Notice of Allowance is awaited.

Should any small matters remain outstanding, the Examiner is encouraged to telephone applicants' undersigned attorney so that the same can be resolved without the necessity of an additional action or response thereto.

Respectfully submitted,

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